

III. REMARKS/ARGUMENTS

A. Status of Claims

Claims 38 and 47-56 are currently pending. Claims 1-37 and 39-46 were previously cancelled. Claim 38 has been amended herein without prejudice. It is respectfully submitted that no new matter has been added by virtue of this amendment.

B. The Recited Transitional Phrase

In the Office Action, the Examiner stated that “the phrase 'consisting essentially of' is not a close-ended transitional phrase that excludes any other materials that are not recited in the claim.”

In response, the Examiner is directed to claim 38, which has been amended to recite “consisting of” in place of “consisting essentially of.” Further, claim 38 has also been amended to specifically recite that the claimed method of treatment utilizing “two analgesic compounds consisting of the recited agents (i.e., celecoxib and oxycodone, and/or their respective salts). Applicants further note that the Abstract has been amended to include the term “consisting.”

The Examiner further stated that the claims recite the term “comprising” and are therefore “open-ended”. In response, Applicants note that the term “comprising” is open ended with respect to the dosage form utilized in the claimed method, with the exclusion that the dosage form is open ended to other analgesics. Applicants note that the analgesic limitation is closed ended by virtue of the “consisting of” terminology of the claims. Applicants respectfully submit that it is not inconsistent for a claim to recite “comprising” and to further recite “consisting of” with respect to a sub-element.

C. Rejection under 35 U.S.C. 103 (a) over Baker et al. and Penning et al.

In the Office Action, the Examiner rejected claims 38, 47-48, 50-56 under 35 U.S.C. 103 (a) over US 4,569,937 (hereinafter "the Baker reference") and Penning et al., J. Med. Chem. Vol. 40(9) (April 1997) pp. 1347-1365 (hereinafter "the Penning reference").

1. The Applicants did not address the references individually in the previous response

Initially, the Examiner has taken the position that Applicants' previous arguments attacked references "individually". Applicants respectfully disagree with the Examiner's position and submit that a combination of the references was addressed in the previous office action.

Applicants note that in arguing a rejection based on a combination of references, it is proper to discuss the teachings of one reference and then to argue how the description of the second reference fails to cure then deficiencies of the first reference, or that the second reference is improperly combinable with the first reference. Such an argument is not addressing the references individually. In the present situation, Applicants direct the Examiner's attention to the April 6, 2006 response which discussed the Baker reference and then stated that "...Applicants submit that, as a whole, the Baker reference would steer one of ordinary skill in the art away from combining the Baker reference with the Penning reference to select an NSAID different than ibuprofen (i.e., celecoxib) to combine with oxycodone, for the reasons argued above." Therefore, Applicants respectfully submit that the previous response properly addressed the combination of references and did not attack the references individually.

2. The Baker Reference in view of the Penning Reference

In the Office Action, the Examiner stated that "Baker teaches the advantages such as enhanced analgesic effect by combining narcotic analgesics and NSAID in general", and cited to the Baker reference at column 1, lines 21+. The Examiner further stated that the Baker reference

teaches "the class of drugs that are known as NSAID...", and cited the Baker reference at Col. 1-2.

Applicants note that column 2 of the Baker reference makes no mention of the term "NSAID". Applicants further point out that the relevant portion of column 1 of the Baker reference states that "[t]his patent discloses that the analgesic effect of the combination of a selected NSAID and a selected narcotic analgesic is greater than for either alone." The phrase "this patent" actually refers to U.S. Patent No. 4,464,376 issued to A. Sunshine et al. (hereinafter "Sunshine"). A copy of the Sunshine reference is enclosed herewith as Exhibit A. Applicants note that the two references to the term "NSAID" at column 1, lines 17-27, are the only recitations of the term "NSAID" in the entire patent, and they are with reference to the teachings of the Sunshine reference. Applicants submit that the purported invention in the Sunshine reference is directed to combinations of caffeine and NSAIDs; caffeine and narcotic analgesics; and caffeine and NSAIDs/narcotic analgesics. Applicants respectfully submit that the present claims exclude the presence of caffeine by virtue of the "consisting of" terminology in the claims.

Furthermore, the Examiner's attention is directed to the Sunshine reference at column 14, lines 58-61, which recite "[t]he term 'selected NSAID' as used herein is intended to mean any non-narcotic analgesic/nonsteroidal anti-inflammatory compound **falling within one of the five structural categories indicated hereinabove.**" (Emphasis added).

These five categories are set forth at column 7, lines 42-50 of the Sunshine reference which states that:

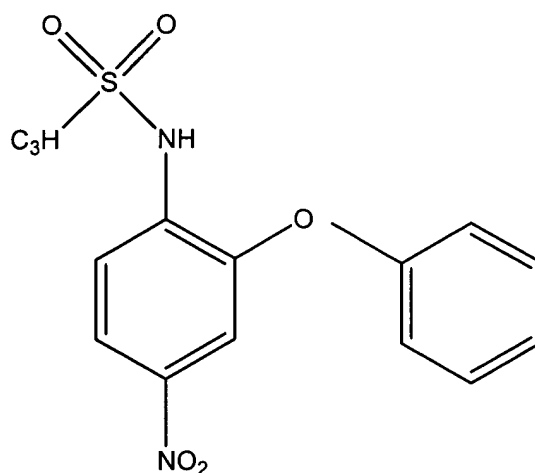
The non-narcotic analgesics/nonsteroidal anti-inflammatory drugs for use in the compositions and methods of the present invention can be selected from the following categories:

- (1) the propionic acid derivatives;
- (2) the acetic acid derivatives;
- (3) the fenamic acid derivatives;

- (4) the biphenylcarboxylic acid derivatives; and
- (5) the oxicams.

The chemical structures of the (5) categories are exemplified in columns 8-11.

Applicants submit that the chemical structure of the presently claimed NSAID, *i.e.* celecoxib:



does not fall within any of the five structural categories indicated above. Therefore, even assuming *arguendo* that the Baker reference contemplates the use of other NSAIDs based on the reference to the Sunshine reference, Applicants submit that the "other" NSAIDs would be limited to the five structural categories listed in the Sunshine reference and would not include celecoxib.

The Examiner further stated that:

...the Baker reference opens the door for developing combinations of NSAIDs and narcotic analgesics beside the combinations of ibuprofen and oxycodone. As discussed above, Baker teaches, in general, a combination of a selected NSAID and a narcotic analgesic would have enhanced analgesic effect (col. 1, lines 22+). Baker et al. also demonstrated a particular combination of the two classes of drug has enhanced analgesic effect. A person of ordinary skill in the art would be motivated to select different NSAID and/or a different narcotic analgesic to form a desired combination with enhanced analgesic effect.

Applicant's respectfully point out that the mention of NSAIDs at column 1, as discussed above, is in reference to the Sunshine reference which describes the enhanced analgesic effect resulting from the combination of NSAIDs with caffeine. Applicants further point out that column 3, lines 19-32, recites the following:

Application of an equieffective dose substitution model and a curvilinear regression analysis utilizing all the data for the individual compounds and various dose ratios for the combinations establishes the existence of unexpectedly enhanced analgesic activity of combinations of oxycodone and ibuprofen, i.e., the resulting activity is greater than the activity expected from the sum of the activities of the individual components.

As can be seen from the above cited passage, the Baker reference does not state that "a combination of a selected NSAID and a narcotic analgesic would have enhanced analgesic effect", as improperly inferred by the Examiner. Rather, the statements in the Baker reference are limited to ibuprofen.

Further, Applicants submit that the Examiner has not shown any motivation to substitute celecoxib for ibuprofen. There is no suggestion in the Baker reference to substitute ibuprofen with any other NSAID, let alone celecoxib. Moreover, the only NSAIDs alluded to in the Baker reference are the NSAIDs which fall into one of the five structural categories described in the Sunshine reference and this reference does not teach or suggest celecoxib.

Furthermore, Applicants submit that the Examiner is applying an improper "obvious to try" rationale in suggesting the substitution of ibuprofen with celecoxib. "In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

Applicants submit that *In re O'Farrell* is analogous to the present situation, where one of ordinary skill in the art would have to try each of numerous possible NSAIDs in place of ibuprofen in order to arrive at the selection of celecoxib, as the Baker reference gives no direction as to what NSAIDs other than ibuprofen would be successful.

The Examiner also stated that "the instant situation is amendable to the type of analysis set forth in *In re Kerkhoven*, wherein the court held that it is *prima facie* obvious to combine two (or more) compositions which is taught by the prior art to be useful for the same purpose. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of applicant's invention to modify the Baker reference analgesic composition by substituting celecoxib for ibuprofen..." (Emphasis Added)(Citations omitted).

Applicants respectfully submit that the Examiner's statements indicate that *In re Kerkhoven* is not being properly applied in rejecting the present claims. As stated by the Examiner, the holding of *In re Kerkhoven* is with respect to combining references. However, the Examiner's rejection, is based on modifying the Baker analgesic composition. Applicants respectfully submit that a combination of the Baker analgesic composition with celecoxib would result in a formulation including a combination of celecoxib and ibuprofen and an opioid analgesic which does not meet the "closed ended" limitation of the present claims with respect to the analgesic composition.

Applicants also submit that the Baker reference teaches away from the use of NSAIDs other than ibuprofen, based on the Baker reference's discussions of the synergistic effect between ibuprofen and narcotic analgesics, and the absolute absence of any reference to other NSAIDs which may be used in the Baker formulation. In further support of this position, the Examiner is respectfully directed to column 1, lines 6 - 9 of the Baker reference which states as follows:

This invention relates to pharmaceutical compositions of narcotic analgesics and ibuprofen having analgesic activity in mammals, and to methods of use of the

compositions to alleviate pain in mammals.
(Emphasis Added)

The Examiner is also directed to column 2, lines 11-15 of the Baker reference which states as follows:

According to the present invention there is provided a pharmaceutical composition comprising a combination of (a) a narcotic analgesic, or a pharmaceutically acceptable salt thereof, and (b) ibuprofen, or a pharmaceutically suitable salt thereof,...
(Emphasis Added).

Applicants further note that ibuprofen is the only NSAID mentioned throughout the entire reference, and it is the only NSAID exemplified in the Baker formulations.

Applicants submit that the Penning reference also fails to teach or suggest the claimed combination of celecoxib and oxycodone. The Examiner stated that "one of ordinary skill in the art would have been motivated to substitute celecoxib for ibuprofen in the Baker reference compositions in light of the Penning reference teaching that celecoxib is analgesically potent with less side effects", however the Examiner is not considering the teaching of the Baker reference as a whole, which is utilizing ibuprofen because of its enhanced analgesic effect when combined with an opioid analgesic. The Penning reference does not suggest that celecoxib would have enhanced analgesic effect when combined with an opioid analgesic, therefore there is no motivation to combine the Penning reference with the Baker reference to substitute ibuprofen with celecoxib in the Baker composition.

In view of the above, Applicants submit that one of ordinary skill in the art not be motivated to substitute the ibuprofen of the formulations of the Baker reference with celecoxib in view of the Penning reference. Applicants further submit that the Baker reference teaches away from the use of all other NSAIDs other than ibuprofen. Accordingly, it is respectfully requested that the 35 U.S.C. 103(a) rejection over the Baker reference and the Penning reference be

removed.

C. Rejection under 35 U.S.C. 103 (a) over Baker et al. and Penning et al. in view of Oshlack et al. (US 5,472,712) or Oshlack et al. (US 6,294,195)

In the Office Action, the Examiner further rejected claim 49 under U.S.C. 103 (a) over Baker et al. and Penning et al. in view of US 5,472,712 (Oshlack et al.) and US 6,294,195 (Oshlack et al.)

This rejection is traversed. For the reasons stated above, Applicants submit that the Baker and Penning references fail to teach or suggest the claimed combination of celecoxib and oxycodone. As the Oshlack reference also fails to teach or suggest the claimed combination of celecoxib and oxycodone, the Oshlack reference fails to cure the deficiencies of the Baker and Penning references.

Accordingly, it is respectfully requested that the 35 U.S.C. 103(a) rejection over the Baker reference, the Penning reference and the Oshlack reference be removed.

III. CONCLUSION

In view of the foregoing, it is believed that the application is now in condition for allowance, and applicants respectfully request such action.

The Examiner is respectfully requested to contact the undersigned at the telephone number provided below in the event that a telephonic interview will advance the prosecution of the application.

Respectfully submitted,

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